

SEQUENCE LISTING

<110> Lambeth, J. David Cheng, Guangjie McCoy, James

<120> Methods and Transgenic Mouse Model for Identifying and Modulating Factors Involved in the Production of Reactive Oxygen Intermediates

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Val Pro Gln Phe Ser Gly Lys Glu Pro Ser Ala Trp Lys Trp Ile Leu Gly Pro Val Val Leu Tyr Ala Cys Glu Arg Ile Ile Arg Phe Trp Arg Phe Gln Gln Glu Val Val Ile Thr Lys Val Val Ser His Pro Ser Gly Val Leu Glu Leu His Met Lys Lys Arg Gly Phe Lys Met Ala Pro Gly Gln Tyr Ile Leu Val Gln Cys Pro Ala Ile Ser Ser Leu Glu Trp His Pro Phe Thr Leu Thr Ser Ala Pro Gln Glu Asp Phe Phe Ser Val His Ile Arg Ala Ala Gly Asp Trp Thr Ala Ala Leu Leu Glu Ala Phe Gly Ala Glu Gly Gln Ala Leu Gln Glu Pro Trp Ser Leu Pro Arg Leu Ala Val Asp Gly Pro Phe Gly Thr Ala Leu Thr Asp Val Phe His Tyr Pro Val Cys Val Cys Val Ala Ala Gly Ile Gly Val Thr Pro Phe Ala Ala Leu Leu Lys Ser Ile Trp Tyr Lys Cys Ser Glu Ala Gln Thr Pro Leu Lys Leu Ser Lys Val Tyr Phe Tyr Trp Ile Cys Arg Asp Ala Arg Ala Phe Glu Trp Phe Ala Asp Leu Leu Ser Leu Glu Thr Arg Met Ser

Glu Gln Gly Lys Thr His Phe Leu Ser Tyr His Ile Phe Leu Thr Gly

465					470					475					480	
Trp	Asp	Glu	Asn	Gln 485	Ala	Leu	His	Ile	Ala 490	Leu	His	Trp	Asp	Glu 495	Asn	
Thr	Asp	Val	Ile 500	Thr	Gly	Leu	Lys	Gln 505	Lys	Thr	Phe	Tyr	Gly 510	Arg	Pro	
Asn	Trp	Asn 515	Asn	Glu	Phe	Lys	Gln 520	Ile	Ala	Tyr	Asn	His 525	Pro	Ser	Ser	
Ser	Ile 530	Gly	Val	Phe	Phe	Cys 535	Gly	Pro	Lys	Ala	Leu 540	Ser	Arg	Thr	Leu	
Gln 545	Lys	Met	Cys	His	Leu 550	Tyr	Ser	Ser	Ala	Asp 555	Pro	Arg	Gly	Val	His 560	
Phe	Tyr	Tyr	Asn	Lys 565	Glu	Ser	Phe									
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gago	cgcag	gcg (eggeg	3999	ec gg	gegge									g ctc Leu	113
											atc Ile					161
	_	_							_		tat Tyr					209
						_	_	_			gga Gly	_	_		_	257

aga gcc tca gca tct gtt ctt aac ctc aac tgc agc ctt atc ctt tta Arg Ala Ser Ala Ser Val Leu Asn Leu Asn Cys Ser Leu Ile Leu Leu ccc atg tgc cga aca ctc ttg gct tac ctc cga gga tca cag aag gtt Pro Met Cys Arg Thr Leu Leu Ala Tyr Leu Arg Gly Ser Gln Lys Val cca agc agg aga acc agg aga ttg ttg gat aaa agc aga aca ttc cat Pro Ser Arg Arg Thr Arg Arg Leu Leu Asp Lys Ser Arg Thr Phe His att acc tgt ggt gtt act atc tgt att ttc tca ggc gtg cat gtg gct Ile Thr Cys Gly Val Thr Ile Cys Ile Phe Ser Gly Val His Val Ala gcc cat ctg gtg aat gcc ctc aac ttc tca gtg aat tac agt gaa gac Ala His Leu Val Asn Ala Leu Asn Phe Ser Val Asn Tyr Ser Glu Asp ttt gtt gaa ctg aat gca gca aga tac cga gat gag gat cct aga aaa Phe Val Glu Leu Asn Ala Ala Arg Tyr Arg Asp Glu Asp Pro Arg Lys ctt ctc ttc aca act gtt cct ggc ctg aca ggg gtc tgc atg gtg gtg Leu Leu Phe Thr Thr Val Pro Gly Leu Thr Gly Val Cys Met Val Val gtg cta ttc ctc atg atc aca gcc tct aca tat gca ata aga gtt tct Val Leu Phe Leu Met Ile Thr Ala Ser Thr Tyr Ala Ile Arg Val Ser aac tat gat atc ttc tgg tat act cat aac ctc ttc ttt gtc ttc tac Asn Tyr Asp Ile Phe Trp Tyr Thr His Asn Leu Phe Phe Val Phe Tyr atg ctg ctg acg ttg cat gtt tca gga ggg ctg ctg aag tat caa act Met Leu Leu Thr Leu His Val Ser Gly Gly Leu Leu Lys Tyr Gln Thr aat tta gat acc cac cct ccc ggc tgc atc agt ctt aac cga acc agc Asn Leu Asp Thr His Pro Pro Gly Cys Ile Ser Leu Asn Arg Thr Ser tct cag aat att tcc tta cca gag tat ttc tca gaa cat ttt cat gaa Ser Gln Asn Ile Ser Leu Pro Glu Tyr Phe Ser Glu His Phe His Glu cct ttc cct gaa gga ttt tca aaa ccg gca gag ttt acc cag cac aaa Pro Phe Pro Glu Gly Phe Ser Lys Pro Ala Glu Phe Thr Gln His Lys ttt gtg aag att tgt atg gaa gag ccc aga ttc caa gct aat ttt cca

Phe	Val	Lys	Ile	Cys 270	Met	Glu	Glu	Pro	Arg 275	Phe	Gln	Ala	Asn	Phe 280	Pro	
						tct Ser			-	_	_		_	_	_	977
						cgg Arg	_		_		_				_	1025
						gat Asp 320										1073
						ggt Gly										1121
						cat His										1169
						gjå aaa										1217
						tta Leu										1265
_		_				caa Gln 400		_				_	_			1313
						cca Pro										1361
						ggc										1409
						gac Asp										1457
						aga Arg			-			_			_	1505
						cat His 480										1553

gac tat gtc aac atc cag ctg tac ctc agt caa aca gat ggg ata cag Asp Tyr Val Asn Ile Gln Leu Tyr Leu Ser Gln Thr Asp Gly Ile Gln 490 495 500 505	1601
aag ata att gga gaa aaa tat cat gca ctg aat tca aga ctg ttt ata Lys Ile Ile Gly Glu Lys Tyr His Ala Leu Asn Ser Arg Leu Phe Ile 510 515 520	1649
gga cgt cct cgg tgg aaa ctt ttg ttt gat gaa ata gca aaa tat aac Gly Arg Pro Arg Trp Lys Leu Leu Phe Asp Glu Ile Ala Lys Tyr Asn 525 530 535	1697
aga gga aaa aca gtt ggt gtt ttc tgt tgt gga ccc aat tca cta tcc Arg Gly Lys Thr Val Gly Val Phe Cys Cys Gly Pro Asn Ser Leu Ser 540 545 550	1745
aag act ctt cat aaa ctg agt aac cag aac aac tca tat ggg aca aga Lys Thr Leu His Lys Leu Ser Asn Gln Asn Asn Ser Tyr Gly Thr Arg 555 560 565	1793
ttt gaa tac aat aaa gag tct ttc agc tga aaacttttgc catgaagcag Phe Glu Tyr Asn Lys Glu Ser Phe Ser 570 575	1843
gactctaaag aaggaatgag tgcaatttct aagactttga aactcagcgg aatcaatcag	1903
ctgtgttatg ccaaagaata gtaaggtttt cttatttatg attatttgaa aatggaaatg	1963
tgagaatgtg gcaacatgac cgtcacatta catgtttaat ctggaaacca aagagaccct	2023
gaagaatatt tgatgtgatg attcattttc agttctcaaa ttaaaagaaa actgttagat	2083
gcacactgtt gattttcatg gtggattcaa gaactcccta gtgaggagct gaacttgctc	2143
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Leu Cys Leu Phe Ile Trp Leu Ser Met Asn Val Leu Leu Phe Trp Lys 20 25 30

Thr Phe Leu Leu Tyr Asn Gln Gly Pro Glu Tyr His Tyr Leu His Gln

35 40 45

Met Leu Gly Leu Cys Leu Ser Arg Ala Ser Ala Ser Val Leu 50 55 60

Asn Leu Asn Cys Ser Leu Ile Leu Leu Pro Met Cys Arg Thr Leu Leu 65 70 75 80

Ala Tyr Leu Arg Gly Ser Gln Lys Val Pro Ser Arg Arg Thr Arg Arg 85 90 95

Leu Leu Asp Lys Ser Arg Thr Phe His Ile Thr Cys Gly Val Thr Ile 100 105 110

Cys Ile Phe Ser Gly Val His Val Ala Ala His Leu Val Asn Ala Leu 115 120 125

Asn Phe Ser Val Asn Tyr Ser Glu Asp Phe Val Glu Leu Asn Ala Ala 130 135 140

Arg Tyr Arg Asp Glu Asp Pro Arg Lys Leu Leu Phe Thr Thr Val Pro 145 150 155 160

Gly Leu Thr Gly Val Cys Met Val Val Leu Phe Leu Met Ile Thr 165 170 175

Ala Ser Thr Tyr Ala Ile Arg Val Ser Asn Tyr Asp Ile Phe Trp Tyr 180 185 190

Thr His Asn Leu Phe Phe Val Phe Tyr Met Leu Leu Thr Leu His Val 195 200 205

Ser Gly Gly Leu Leu Lys Tyr Gln Thr Asn Leu Asp Thr His Pro Pro 210 215 220

Gly Cys Ile Ser Leu Asn Arg Thr Ser Ser Gln Asn Ile Ser Leu Pro 225 230 235 240

Glu Tyr Phe Ser Glu His Phe His Glu Pro Phe Pro Glu Gly Phe Ser 245 250 255

Lys Pro Ala Glu Phe Thr Gln His Lys Phe Val Lys Ile Cys Met Glu 260 265 270

Glu Pro Arg Phe Gln Ala Asn Phe Pro Gln Thr Trp Leu Trp Ile Ser 275 280 285

Gly Pro Leu Cys Leu Tyr Cys Ala Glu Arg Leu Tyr Arg Tyr Ile Arg 290 295 300

Ser Asn Lys Pro Val Thr Ile Ile Ser Val Ile Ser His Pro Ser Asp 305 310 315 320

Val Met Glu Ile Arg Met Val Lys Glu Asn Phe Lys Ala Arg Pro Gly 325 330 335

Gln Tyr Ile Thr Leu His Cys Pro Ser Val Ser Ala Leu Glu Asn His 340 345 350

Pro Phe Thr Leu Thr Met Cys Pro Thr Glu Thr Lys Ala Thr Phe Gly 355 360 365

Val His Leu Lys Ile Val Gly Asp Trp Thr Glu Arg Phe Arg Asp Leu 370 375 380

Leu Leu Pro Pro Ser Ser Gln Asp Ser Glu Ile Leu Pro Phe Ile Gln 385 390 395 400

Ser Arg Asn Tyr Pro Lys Leu Tyr Ile Asp Gly Pro Phe Gly Ser Pro 405 410 415

Phe Glu Glu Ser Leu Asn Tyr Glu Val Ser Leu Cys Val Ala Gly Gly
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Ile Gly Val Thr Pro Phe Ala Ser Ile Leu Asn Thr Leu Leu Asp Asp 435 440 445

Trp Lys Pro Tyr Lys Leu Arg Arg Leu Tyr Phe Ile Trp Val Cys Arg
450 455

Asp Ile Gln Ser Phe Arg Trp Phe Ala Asp Leu Leu Cys Met Leu His 465 470 475 480

Asn Lys Phe Trp Gln 485	Glu Asn Arg	Pro Asp Tyr 490		Gln Leu 495
Tyr Leu Ser Gln Thr 500	_ _	Gln Lys Ile 505	Ile Gly Glu : 510	Lys Tyr
His Ala Leu Asn Ser 515	Arg Leu Phe 520	Ile Gly Arg	Pro Arg Trp : 525	Lys Leu
Leu Phe Asp Glu Ile 530	Ala Lys Tyr 535		Lys Thr Val (540	Gly Val
Phe Cys Cys Gly Pro 545	Asn Ser Leu 550	Ser Lys Thr : 555	Leu His Lys I	Leu Ser 560
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gcc ccc gcc ccc cgc Ala Pro Ala Pro Arg 15		Arg Arg Pro I		
gcc tac tgg cac aac Ala Tyr Trp His Asn 30				
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						atc Ile										351
		_		_	_	tgg Trp 100	_	_		_			_	_	_	399
						ctt Leu					-	-		-		447
					_	cac His					_		_	_	_	495
						cag Gln										543
						cac His										591
						ctc Leu 180	_			-		_		_		639
_		_				gag Glu							_			687
						ctc Leu									_	735
						atc Ile										783
						gca Ala										831
						cat His 260										879

		_			_	tac Tyr	_		_						_	927
_						ttc Phe			_	_	_			_		975
-				_		att Ile					_					1023
_					_	gca Ala		-		_		_			_	1071
	_	_		_		aca Thr 340	_	_	_	_			_		_	1119
					_	gag Glu					_			_	_	1167
		-				gjà aaa				_				_		1215
		_				gly aaa	_								_	1263
		_	_	_		atg Met				_		_	_			1311
_		_	_	_		tcc Ser 420			_		_		_		_	1359
_			_		_	ttt Phe					_	_	_			1407
						ctg Leu										1455
		_				cgc Arg		_		_		_		_		1503
						gac Asp										1551

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aaa gtg gct gct gag aag aa Lys Val Ala Ala Glu Lys Ly 530			
tcc cca gct ctg gcc aag gt Ser Pro Ala Leu Ala Lys Va 545			1743
ttc aga ttt ttc caa gag aa Phe Arg Phe Phe Gln Glu As 560	·-	ctct ccaagctctg	1790
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Pro Arg Pro Arg Pro Arg Pro Arg Gln Leu Thr Arg Ala Tyr Trp
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His Asn His Arg Ser Gln Leu Phe Cys Leu Ala Thr Tyr Ala Gly Leu 35 40 45

His Val Leu Leu Phe Gly Leu Ala Ala Ser Ala His Arg Asp Leu Gly 50 55 60

Ala Ser Val Met Val Ala Lys Gly Cys Gly Gln Cys Leu Asn Phe Asp 65 70 75 80

Cys Ser Phe Ile Ala Val Leu Met Leu Arg Arg Cys Leu Thr Trp Leu 85 90 95

Arg Ala Thr Trp Leu Ala Gln Val Leu Pro Leu Asp Gln Asn Ile Gln
100 105 110

Phe His Gln Leu Met Gly Tyr Val Val Gly Leu Ser Leu Val His 115 120 125

Thr Val Ala His Thr Val Asn Phe Val Leu Gln Ala Gln Ala Glu Ala 130 135 140

Ser Pro Phe Gln Phe Trp Glu Leu Leu Leu Thr Thr Arg Pro Gly Ile 145 150 155 160

Gly Trp Val His Gly Ser Ala Ser Pro Thr Gly Val Ala Leu Leu Leu 165 170 175

Leu Leu Leu Met Phe Ile Cys Ser Ser Ser Cys Ile Arg Arg Ser 180 185 190

Gly His Phe Glu Val Phe Tyr Trp Thr His Leu Ser Tyr Leu Leu Val 195 200 205

Trp Leu Leu Ile Phe His Gly Pro Asn Phe Trp Lys Trp Leu Leu 210 215 220

Val Pro Gly Ile Leu Phe Phe Leu Glu Lys Ala Ile Gly Leu Ala Val 225 230 235 240

Ser Arg Met Ala Ala Val Cys Ile Met Glu Val Asn Leu Leu Pro Ser 245 250 255

Lys Val Thr His Leu Leu Ile Lys Arg Pro Pro Phe Phe His Tyr Arg

Pro Gly Asp Tyr Leu Tyr Leu Asn Ile Pro Thr Ile Ala Arg Tyr Glu Trp His Pro Phe Thr Ile Ser Ser Ala Pro Glu Gln Lys Asp Thr Ile Trp Leu His Ile Arg Ser Gln Gly Gln Trp Thr Asn Arg Leu Tyr Glu Ser Phe Lys Ala Ser Asp Pro Leu Gly Arg Gly Ser Lys Arg Leu Ser Arg Ser Val Thr Met Arg Lys Ser Gln Arg Ser Ser Lys Gly Ser Glu Ile Leu Leu Glu Lys His Lys Phe Cys Asn Ile Lys Cys Tyr Ile Asp Gly Pro Tyr Gly Thr Pro Thr Arg Arg Ile Phe Ala Ser Glu His Ala Val Leu Ile Gly Ala Gly Ile Gly Ile Thr Pro Phe Ala Ser Ile Leu Gln Ser Ile Met Tyr Arg His Gln Lys Arg Lys His Thr Cys Pro Ser Cys Gln His Ser Trp Ile Glu Gly Val Gln Asp Asn Met Lys Leu His Lys Val Asp Phe Ile Trp Ile Asn Arg Asp Gln Arg Ser Phe Glu Trp Phe Val Ser Leu Leu Thr Lys Leu Glu Met Asp Gln Ala Glu Glu Ala Gln Tyr Gly Arg Phe Leu Glu Leu His Met Tyr Met Thr Ser Ala Leu

Gly Lys Asn Asp Met Lys Ala Ile Gly Leu Gln Met Ala Leu Asp Leu 485 490 495	
Leu Ala Asn Lys Glu Lys Lys Asp Ser Ile Thr Gly Leu Gln Thr Arg 500 505 510	
Thr Gln Pro Gly Arg Pro Asp Trp Ser Lys Val Phe Gln Lys Val Ala 515 520 525	
Ala Glu Lys Lys Gly Lys Val Gln Val Phe Phe Cys Gly Ser Pro Ala 530 535 540	
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agaceteage etagteteet gateeecaag cagggeeetg eetaaggaae acaetetgea	240
gagtgctggg ccaaagcagg gttttccaac taatcttaga aggtaaagtc catgaagggt	300
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tgc ctg gct cta gca tgg aca ctt ctg gtt ggg gca tgg acc cct ctg Cys Leu Ala Leu Ala Trp Thr Leu Leu Val Gly Ala Trp Thr Pro Leu 5 10 15	403
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_	-	_	_		gcc Ala	_		_	_				_		_	<u> </u>	547
	_			_	ccc Pro			_	_		_					5	595
					ctg Leu									_		6	543
					cac His 105								-	-		€	591
					gag Glu							_			_	7	739
					gac Asp											7	787
					ccc Pro											8	335
					gtg Val											8	383
					tgg Trp 185											9	31
					ccc Pro											9	79
					gcg Ala											10	27
					gcc Ala											10	75
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Phe	Leu 245	Gln	Ala	Leu	Gly	Leu 250	Leu	Trp	Phe	Arg	Tyr 255	His	Asn	Leu	Trp	
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					aag Lys											1219
					ccc Pro			_	_				_			1267
					ttt Phe											1315
					ttc Phe											1363
					tgc Cys 345											1411
					ctc Leu											1459
					agt Ser	_	_	_			_	_	_	-		1507
					gca Ala											1555
					cct Pro											1603
					cag Gln 425											1651
					gca Ala											1699
					ctc Leu				Asn	_		-	_		_	1747

			cag Gln								1795
			cac His 490	-	-			_	_		1843
			gtg Val								1891
			glà aaa	_		_	_		_	_	1939
			cag Gln								1987
			ccc Pro								2035
			cag Gln 570					-	_	_	2083
			gac Asp			 	_				2131
			ctc Leu								2179
			cgg Arg								2227
			agc Ser								2275
			caa Gln 650								2323
			gly aaa								2371
			cag Gln								2419

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								_	_	_		agc Ser		_	_	2563
					_			_		_	_	aga Arg	-	_		2611
												ttc Phe				2659
												gjå aaa				2707
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	-			_			_			_		cag Gln	-	_		2803
Val 820	Glu	Ser	Met	Phe	Ser 825	Leu	Ala	Asp	Lys	Asp 830	Gly	aat Asn	Gly	Tyr	Leu 835	2851
Ser	Phe	Arg	Glu	Phe 840	Leu	Asp	Ile	Leu	Val 845	Val	Phe	atg Met	Lys	Gly 850	Ser	2899
			-		_		_		_	_		gac Asp		-		2947
Asn	Gly	Leu 870	Ile	Ser	Lys	Asp	Glu 875	Phe	Ile	Arg	Met	ctg Leu 880	Arg	Ser	Phe	2995
												ctg Leu				3043
												aag Lys				3091

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		ggg gtg gag gtg Gly Val Glu Val 940		7
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		tgt tcc cgc agc Cys Ser Arg Ser 975		3
		tgc ccc atg gac Cys Pro Met Asp 990	_	1
cag gag att cgg Gln Glu Ile Arg		c aag aag gta ac y Lys Lys Val Th 1005	_	6
ccc ttg ctg ttc Pro Leu Leu Phe		c cga gag aag tt s Arg Glu Lys Ph 1020		1
		g ttc aag cgc tt n Phe Lys Arg Pho 1035		6
tac cgg cgc cac Tyr Arg Arg His		g gcc gtg ttc ta L Ala Val Phe Ty 1050		1
		c tac tac tac gc a Tyr Tyr Tyr Ala 1065		6
		c acc cgc gtg gga Thr Arg Val Gl		1
		e tot tto atg tto Ser Phe Met Pho 1095		6
ttg ctc acc atg Leu Leu Thr Met		c atc acc ttc cto 1 Ile Thr Phe Let 1110		1
ttc ctc aac cgc	tac gtg ccc tto	gac gcc gcc gtg	g gac ttc cat 373	6

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				gtg Val 1150											3826
-	_			tgc Cys 1165								_	_		3871
				cag Gln 1180	_							_		-	3916
				999 Gly 1195											3961
				tcc Ser 1210											4006
_				cac His 1225					ctg Leu 1230			_	_		4051
				agc Ser 1240		-	_		_	_		-			4096
				gtc Val 1255					tat Tyr 1260	gjå aaa					4141
				cgg Arg 1270											4186
	-	_		tca Ser 1285					_			_			4231
				tac Tyr 1300											4276
				acc Thr 1315											4321

				gac Asp 1330											4366
				cgc Arg 1345							_	_	_		4411
_	_	_	_	aga Arg 1360				_			_				4456
				cag Gln 1375				_							4501
				att Ile 1390											4546
_	_	_		aag Lys 1405			_	_	_				_	-	4591
				atc Ile 1420											4636
				atc Ile 1435					gag Glu 1440		aat Asn				4681
				gtg Val 1450					acc Thr 1455		ctg Leu				4726
				acc Thr 1465							gag Glu				4771
Gln	Lys	Val	Leu	aac Asn 1480	Arg	Ser	Leu	Phe	Thr 1485	Gly	Leu	Arg	Ser	Ile 1490	4816
				cgt Arg 1495											4861
				ccc Pro 1510											4906
				atg Met		_			-	_	-	_	_		4951

atc aac agg Ile Asn Arg				ac cat tat gag is His Tyr Gl	
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Gln Pro Leu Gly Glu Pro His Leu Pro Asn Pro Arg Asp Leu Ser Asn 65 70 75 80

Thr Ile Ser Arg Gly Pro Ala Gly Leu Ala Ser Leu Arg Asn Arg Thr 85 90 95

Val Leu Gly Val Phe Phe Gly Tyr His Val Leu Ser Asp Leu Val Ser 100 105 110

Val Glu Thr Pro Gly Cys Pro Ala Glu Phe Leu Asn Ile Arg Ile Pro 115 120 125

Pro Gly Asp Pro Met Phe Asp Pro Asp Gln Arg Gly Asp Val Val Leu 130 135 140

Pro Phe Gln Arg Ser Arg Trp Asp Pro Glu Thr Gly Arg Ser Pro Ser 145 150 155 160

Asn Pro Arg Asp Pro Ala Asn Gln Val Thr Gly Trp Leu Asp Gly Ser 165 170 175

Ala Ile Tyr Gly Ser Ser His Ser Trp Ser Asp Ala Leu Arg Ser Phe 180 185 190

Ser Arg Gly Gln Leu Ala Ser Gly Pro Asp Pro Ala Phe Pro Arg Asp 195 200 205

Ser Gln Asn Pro Leu Leu Met Trp Ala Ala Pro Asp Pro Ala Thr Gly 210 215 220

Gln Asn Gly Pro Arg Gly Leu Tyr Ala Phe Gly Ala Glu Arg Gly Asn 225 230 235 240

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Asn Ile Ala Val Tyr Glu Trp Leu Pro Ser Phe Leu Gln Lys Thr Leu 290 295 300

Pro Glu Tyr Thr Gly Tyr Arg Pro Phe Leu Asp Pro Ser Ile Ser Ser 305 310 315 320

Glu Phe Val Ala Ala Ser Glu Gln Phe Leu Ser Thr Met Val Pro Pro 325 330 335

Gly Val Tyr Met Arg Asn Ala Ser Cys His Phe Gln Gly Val Ile Asn 340 345 350

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Leu Leu Gly Met Ala Ser Gln Ile Ala Glu Arg Glu Asp His Val Leu 385 390 395 400

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Thr Asp His Leu Ala Ser Cys Leu Gln Arg Gly Arg Asp Leu Gly Leu 420 425 430

Pro Ser Tyr Thr Lys Ala Arg Ala Ala Leu Gly Leu Ser Pro Ile Thr 435 440 445

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Leu Leu Pro Gly Gly Leu Leu Glu Ser His Arg Asp Pro Gly Pro Leu 485 490 495

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Arg Tyr Trp Phe Glu Asn Thr Arg Asn Gly Leu Phe Ser Lys Lys Glu 515 520 525

Ile Glu Glu Ile Arg Asn Thr Thr Leu Gln Asp Val Leu Val Ala Val 530 535 540

Ile Asn Ile Asp Pro Ser Ala Leu Gln Pro Asn Val Phe Val Trp His 545 550 555 560

Lys Gly Asp Pro Cys Pro Gln Pro Arg Gln Leu Ser Thr Glu Gly Leu 565 570 575

Pro Ala Cys Ala Pro Ser Val Val Arg Asp Tyr Phe Glu Gly Ser Gly 580 585 590

Phe Gly Phe Gly Val Thr Ile Gly Thr Leu Cys Cys Phe Pro Leu Val 595 600 605

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Lys Arg Leu Gln Gly Gln Asp Arg Gln Ser Ile Val Ser Glu Lys Leu 625 630 635 640

Val Gly Gly Met Glu Ala Leu Glu Trp Gln Gly His Lys Glu Pro Cys 645 650 655

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660 665 670

Gly Arg Leu Thr Val Leu Arg Thr Ile Gln Leu Gln Pro Pro Gln Lys 675 680 685

Val Asn Phe Val Leu Ser Ser Asn Arg Gly Arg Arg Thr Leu Leu Leu 690 695 700

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Gly Leu Ser Ile Gln Glu Trp Glu Leu Arg Glu Gln Glu Leu Met Arg Ala Ala Val Thr Arg Glu Gln Arg Arg His Leu Leu Glu Thr Phe Phe Arg His Leu Phe Ser Gln Val Leu Asp Ile Asn Gln Ala Asp Ala Gly Thr Leu Pro Leu Asp Ser Ser Gln Lys Val Arg Glu Ala Leu Thr Cys Glu Leu Ser Arg Ala Glu Phe Ala Glu Ser Leu Gly Leu Lys Pro Gln Asp Met Phe Val Glu Ser Met Phe Ser Leu Ala Asp Lys Asp Gly Asn Gly Tyr Leu Ser Phe Arg Glu Phe Leu Asp Ile Leu Val Val Phe Met Lys Gly Ser Pro Glu Glu Lys Ser Arg Leu Met Phe Arg Met Tyr Asp Phe Asp Gly Asn Gly Leu Ile Ser Lys Asp Glu Phe Ile Arg Met Leu Arg Ser Phe Ile Glu Ile Ser Asn Asn Cys Leu Ser Lys Ala Gln Leu Ala Glu Val Val Glu Ser Met Phe Arg Glu Ser Gly Phe Gln Asp Lys Glu Glu Leu Thr Trp Glu Asp Phe His Phe Met Leu Arg Asp His Asn Ser Glu Leu Arg Phe Thr Gln Leu Cys Val Lys Gly Val Glu Val Pro

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- Met Ile Cys Pro Ser Pro Arg Val Ser Ala Arg Cys Ser Arg Ser Asp 965 970 975
- Ile Glu Thr Glu Leu Thr Pro Gln Arg Leu Gln Cys Pro Met Asp Thr 980 985 990
- Asp Pro Pro Gln Glu Ile Arg Arg Phe Gly Lys Lys Val Thr Ser 995 1000 1005
- Phe Gln Pro Leu Leu Phe Thr Glu Ala His Arg Glu Lys Phe Gln 1010 1015 1020
- Arg Ser Cys Leu His Gln Thr Val Gln Gln Phe Lys Arg Phe Ile 1025 1030 1035
- Glu Asn Tyr Arg Arg His Ile Gly Cys Val Ala Val Phe Tyr Ala 1040 1045 1050
- Ile Ala Gly Gly Leu Phe Leu Glu Arg Ala Tyr Tyr Ala Phe 1055 1060 1065
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- Glu Thr Phe Leu Asn Arg Tyr Val Pro Phe Asp Ala Ala Val Asp 1115 1120 1125
- Phe His Arg Leu Ile Ala Ser Thr Ala Ile Val Leu Thr Val Leu 1130 1135 1140
- His Ser Val Gly His Val Val Asn Val Tyr Leu Phe Ser Ile Ser 1145 1150 1155

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- Thr Val Pro Gly Leu Thr Gly Val Val Leu Leu Leu Ile Leu Ala 1190 1195 1200
- Ile Met Tyr Val Phe Ala Ser His His Phe Arg Arg Ser Phe 1205 1210 1215
- Arg Gly Phe Trp Leu Thr His His Leu Tyr Ile Leu Leu Tyr Val 1220 1225 1230
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- Thr Ser Ala Pro His Glu Asp Thr Leu Ser Leu His Ile Arg Ala 1325 1330 1335
- Ala Gly Pro Trp Thr Thr Arg Leu Arg Glu Ile Tyr Ser Ala Pro 1340 1345 1350
- Thr Gly Asp Arg Cys Ala Arg Tyr Pro Lys Leu Tyr Leu Asp Gly 1355 1360 1365

Pro Phe Gly Glu Gly His Gln Glu Trp His Lys Phe Glu Val Ser 1370 1375 1380

Val Leu Val Gly Gly Gly Ile Gly Val Thr Pro Phe Ala Ser Ile 1385 1390 1395

Leu Lys Asp Leu Val Phe Lys Ser Ser Val Ser Cys Gln Val Phe 1400 1405 1410

Cys Lys Lys Ile Tyr Phe Ile Trp Val Thr Arg Thr Gln Arg Gln 1415 1420 1425

Phe Glu Trp Leu Ala Asp Ile Ile Arg Glu Val Glu Glu Asn Asp 1430 1435 1440

His Gln Asp Leu Val Ser Val His Ile Tyr Ile Thr Gln Leu Ala 1445 1450 1455

Glu Lys Phe Asp Leu Arg Thr Thr Met Leu Tyr Ile Cys Glu Arg 1460 1465 1470

His Phe Gln Lys Val Leu Asn Arg Ser Leu Phe Thr Gly Leu Arg 1475 1480 1485

Ser Ile Thr His Phe Gly Arg Pro Pro Phe Glu Pro Phe Phe Asn 1490 1495 1500

Ser Leu Gln Glu Val His Pro Gln Val Arg Lys Ile Gly Val Phe 1505 1510 1515

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140

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Arg	Asn	Ala	Ser 350	Cys	His	ttc Phe	Arg	Lys 355	Val	Leu	Asn	Lys	Gly 360	Phe	Gln	1289
						gtc Val										1337

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					ggc Gly											:	2105
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					cag Gln			_	_	_				_		2	2297
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					ctg Leu											2	2537
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	_	cga Arg 1110					aac Asn 1115	_					_	-	3569
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							cat His						atc Ile	_	3929

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Ile	Arg	Ala 1335	Val	Gly	Pro	Trp	Thr 1340	Thr	Arg	Leu	Arg	gag Glu 1345	Ile	Tyr	4244
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Leu	Asp	Gly 1365	Pro	Phe	Gly	Glu	Gly 1370	His	Gln	Glu	Trp	cat His 1375	Lys	Phe	4334
Glu	Val	Ser 1380	Val	Leu	Val	Gly	Gly 1385	Gly	Ile	Gly	Val	acc Thr 1390	Pro	Phe	4379
Ala	Ser	Ile 1395	Leu	Lys	Asp	Leu	Val 1400	Phe	Lys	Ser	Ser	ttg Leu 1405	Gly	Ser	4424
Gln	Met	Leu 1410	Cys	Lys	Lys	Ile	Tyr 1415	Phe	Ile	Trp	Val	aca Thr 1420	Arg	Thr	4469
Gln	Arg	Gln 1425	Phe	Glu	Trp	Leu	Ala 1430	Asp	Ile	Ile	Gln	gag Glu 1435	Val	Glu	4514
gag	aac	gac	cac	cag	gac	ctg	gtg	tct	gtg	cac	att	tat	gtc	acc	4559

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Ser Leu His Asn Arg Thr Val Leu Gly Val Phe Phe Gly Tyr His Val Leu Ser Asp Val Val Ser Val Glu Thr Pro Gly Cys Pro Ala Glu Phe Leu Asn Ile Arg Ile Pro Pro Gly Asp Pro Val Phe Asp Pro Asp Gln Arg Gly Asp Val Val Leu Pro Phe Gln Arg Ser Arg Trp Asp Pro Glu Thr Gly Arg Ser Pro Ser Asn Pro Arg Asp Leu Ala Asn Gln Val Thr Gly Trp Leu Asp Gly Ser Ala Ile Tyr Gly Ser Ser His Ser Trp Ser Asp Ala Leu Arg Ser Phe Ser Gly Gly Gln Leu Ala Ser Gly Pro Asp Pro Ala Phe Pro Arg Asp Ser Gln Asn Pro Leu Leu Met Trp Ala Ala Pro Asp Pro Ala Thr Gly Gln Asn Gly Pro Arg Gly Leu Tyr Ala Phe Gly Ala Glu Arg Gly Asn Arg Glu Pro Phe Leu Gln Ala Leu Gly Leu Leu Trp Phe Arg Tyr His Asn Leu Trp Ala Gln Arg Leu Ala Arg Gln His Pro Asp Trp Glu Asp Glu Glu Leu Phe Gln His Ala Arg Lys Arg

Val Ile Ala Thr Tyr Gln Asn Ile Ala Val Tyr Glu Trp Leu Pro Ser

Phe Leu Gln Lys Thr Leu Pro Glu Tyr Thr Gly Tyr Arg Pro Phe Leu 305 310 315

Asp Pro Ser Ile Ser Pro Glu Phe Val Val Ala Ser Glu Gln Phe Phe 325 330 335

Ser Thr Met Val Pro Pro Gly Val Tyr Met Arg Asn Ala Ser Cys His 340 345 350

Phe Arg Lys Val Leu Asn Lys Gly Phe Gln Ser Ser Gln Ala Leu Arg 355 360 365

Val Cys Asn Asn Tyr Trp Ile Arg Glu Asn Pro Asn Leu Asn Ser Thr 370 375 380

Gln Glu Val Asn Glu Leu Leu Leu Gly Met Ala Ser Gln Ile Ser Glu 385 390 395 400

Leu Glu Asp Asn Ile Val Val Glu Asp Leu Arg Asp Tyr Trp Pro Gly 405 410 415

Pro Gly Lys Phe Ser Arg Thr Asp Tyr Val Ala Ser Ser Ile Gln Arg 420 425 430

Gly Arg Asp Met Gly Leu Pro Ser Tyr Ser Gln Ala Leu Leu Ala Phe 435 440 445

Gly Leu Asp Ile Pro Arg Asn Trp Ser Asp Leu Asn Pro Asn Val Asp 450 455 460

Pro Gln Val Leu Glu Ala Thr Ala Ala Leu Tyr Asn Gln Asp Leu Ser 465 470 475 480

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Asp Gly Asp Arg Tyr Trp Phe Glu Asn Thr Arg Asn Gly Leu Phe Ser 515 520 525

Lys Lys Glu Ile Glu Asp Ile Arg Asn Thr Thr Leu Arg Asp Val Leu 530 535 540

Val Ala Val Ile Asn Ile Asp Pro Ser Ala Leu Gln Pro Asn Val Phe 545 550 555 560

Val Trp His Lys Gly Ala Pro Cys Pro Gln Pro Lys Gln Leu Thr Thr 565 570 575

Asp Gly Leu Pro Gln Cys Ala Pro Leu Thr Val Leu Asp Phe Phe Glu 580 585 590

Gly Ser Ser Pro Gly Phe Ala Ile Thr Ile Ile Ala Leu Cys Cys Leu 595 600 605

Pro Leu Val Ser Leu Leu Ser Gly Val Val Ala Tyr Phe Arg Gly 610 615 620

Arg Glu His Lys Lys Leu Gln Lys Lys Leu Lys Glu Ser Val Lys 625 630 635 640

Glu Ala Ala Lys Asp Gly Val Pro Ala Met Glu Trp Pro Gly Pro Lys
645 650 655

Glu Arg Ser Ser Pro Ile Ile Ile Gln Leu Leu Ser Asp Arg Cys Leu 660 665 670

Gln Val Leu Asn Arg His Leu Thr Val Leu Arg Val Val Gln Leu Gln 675 680 685

Pro Leu Gln Gln Val Asn Leu Ile Leu Ser Asn Asn Arg Gly Cys Arg 690 695 700

Thr Leu Leu Leu Lys Ile Pro Lys Glu Tyr Asp Leu Val Leu Leu Phe 705 710 715 720

Ser Ser Glu Glu Arg Gly Ala Phe Val Gln Gln Leu Trp Asp Phe
725 730 735

Cys Val Arg Trp Ala Leu Gly Leu His Val Ala Glu Met Ser Glu Lys
740 745 750

Glu Leu Phe Arg Lys Ala Val Thr Lys Gln Gln Arg Glu Arg Ile Leu 755 760 765

Glu Ile Phe Phe Arg His Leu Phe Ala Gln Val Leu Asp Ile Asn Gln 770 775 780

Ala Asp Ala Gly Thr Leu Pro Leu Asp Ser Ser Gln Lys Val Arg Glu
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Leu Lys Pro Gln Asp Met Phe Val Glu Ser Met Phe Ser Leu Ala Asp 820 825 830

Lys Asp Gly Asn Gly Tyr Leu Ser Phe Arg Glu Phe Leu Asp Ile Leu 835 840 845

Val Val Phe Met Lys Gly Ser Pro Glu Asp Lys Ser Arg Leu Met Phe 850 855 860

Thr Met Tyr Asp Leu Asp Glu Asn Gly Phe Leu Ser Lys Asp Glu Phe 865 870 875 880

Phe Thr Met Met Arg Ser Phe Ile Glu Ile Ser Asn Asn Cys Leu Ser 885 890 895

Lys Ala Gln Leu Ala Glu Val Val Glu Ser Met Phe Arg Glu Ser Gly 900 905 910

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Arg Asp His Asp Ser Glu Leu Arg Phe Thr Gln Leu Cys Val Lys Gly 930 935 940

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Ser Cys Arg Val Ser Phe Ile Thr Arg Thr Pro Gly Glu Arg Ser His

965 970 975

Pro Gln Gly Leu Gly Pro Pro Ala Pro Glu Ala Pro Glu Leu Gly Gly 980 985 990

- Pro Gly Leu Lys Lys Arg Phe Gly Lys Lys Ala Ala Val Pro Thr Pro 995 1000 1005
- Arg Leu Tyr Thr Glu Ala Leu Gln Glu Lys Met Gln Arg Gly Phe 1010 1015 1020
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- Arg Arg His Ile Val Cys Val Ala Ile Phe Ser Ala Ile Cys Val 1040 1045 1050
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- Lys Leu Pro Gln Lys Phe Tyr Trp Trp Phe Phe Gln Thr Val Pro 1175 1180 1185
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- Val Phe Ala Ser His His Phe Arg Arg Arg Ser Phe Arg Gly Phe 1205 1210 1215
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Lys Val Leu Asn Arg Ser Leu Phe Thr Gly Leu Arg Ser Ile Thr 1475 1480

His Phe Gly Arg Pro Pro Phe Glu Pro Phe Asn Ser Leu Gln 1490 1495

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